UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/565,989	05/19/2006	Tanja Wille	QGN-037.1P US	9436

7590 11/14/2008

Leon R Yankwich
Yankwich & Associates
201 Broadway
Cambridge, MA 02139

EXAMINER	
WILDER, CYNTHIA B	
ART UNIT	PAPER NUMBER
1637	
MAIL DATE	DELIVERY MODE
11/14/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/565,989	WILLE ET AL.	
	Examiner	Art Unit	
	CYNTHIA B. WILDER	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 July 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-40* is/are pending in the application.

4a) Of the above claim(s) *34-38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of the claims 1-40 as they relate to the species A and SEQ ID NO: 2 in the reply filed on 8/25/2008 is acknowledged. The traversal is on the ground(s) that the claimed invention shares a unifying special technical feature which confers novelty over the art. Applicant states that the Examiner has not cited any art and therefore has no basis to assert that the species lack a unifying special technical feature, which is defined as technical features that defines the contribution over prior art. Applicant states that the species cited as not relating to a single general inventive concept are merely preferred embodiments of the molecular species for selectively suppressing the reverse transcription of at least one unwanted mRNA to be used in the general inventive concept.

All of the arguments have been thoroughly reviewed and considered, but are not found persuasive because the claims read on structurally distinct chemical compounds in the recitation of the DNA sequences, the PNA sequences, and the LNA sequences, that are capable of separate and distinct use and thus does not relate to a single general inventive concept. Additionally, even though the inventions of the se groups require the technical feature as asserted by Applicant, namely the suppression of reverse transcription, this technical feature is not a special technical feature as it does not make a contribution over the prior art in view of Christians et al (2005/0003369, effective filing date October 2002, which teaches the suppression of reverse transcription (see e.g. abstract, Figure 1 which shows steps of RT-PCR).

2. The requirement is still deemed proper and is therefore made FINAL. Upon further review the SEQ ID NOS 3 will be examined along with the elected SEQ ID NO: 2 as the sequence of SEQ ID NO: 3 encompass the sequence of SEQ ID NO: 2. The claims which read on the elected sequences are claims 1-33, 39 and 40.

3. The claims 34-38, and SEQ ID NOS: 1, 4-33 are withdrawn from consideration as being drawn to a non-elected invention

Claim Rejections - 35 USC § 102(b)

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1, 2, 4-5, 17-21, 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Oemar et al (WO 01/32931, May 2001). Regarding claim 1, Oemar et al teach a process for the reverse transcription and/or amplification of a product of a reverse transcription of a pool of nucleic acids of a type (A) from a biological sample or an enzymatic reaction, said process comprising selectively suppressing the reverse transcription of at least one unwanted nucleic acid of type (A) and/or selectively suppressing the amplification of a product of a reverse transcription of at least one unwanted nucleic acid of type (A) (page 3, lines 12-16 and Example 1 "Inhibition of cDNA synthesis using PNA oligonucleotides).

Regarding claim 2, Oemar et al teach the process according to claim 1, wherein the nucleic acid of type (A) is mRNA (page 4, line 6 and page 5, lines 25-27).

Regarding claim 4, Oemar et al teach the process according to claim 1, further comprising the following steps carrying out a reverse transcription reaction of an RNA from a biological sample or a enzymatic reaction in the presence of at least one oligo-dT primer, and/or carrying out amplification of the cDNA (Example 1).

Regarding claim 5, Oemar et al teach the process according to claim 4, wherein steps a) and/or d) are carried out in the presence of at least one molecular species for selectively suppressing the reverse transcription of at least one unwanted mRNA, while the molecular species prevents the reverse transcription of the unwanted mRNA, and/or for selectively suppressing the amplification of a product of the reverse transcription of at least one unwanted mRNA, the molecular species preventing the amplification of the single-stranded or double-stranded cDNA prepared from the unwanted mRNA (Example 1).

Regarding claim 17, 19-21, Oemar et al teach wherein the molecular species is a DNA oligonucleotide complementary to one of the cDNA strand, and wherein the nucleic acid analogue is PNA; having a length of about 10-30 nucleotides (see Example 1 and Page 5, lines 1-3; see also Figure 1-3).

Regarding claim 24, Oemar et al each wherein the molecular species bind to a region or multiple regions complementary to the 3' end of the RNA molecule (page 5).

Regarding claim 27, Oemar et al teach wherein the molecular species has at its 3' end a modification which prevents elongation from being initialized at the 3' end of the molecular species (Example 1).

Claim Rejections - 35 USC § 102(a)

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

7. Claims 1-12, 17-19, 24-27, 39 and 40 are rejected under 35 U.S.C. 102(e) as being anticipated by Christians et al (US 2005/0003369, effective Filing date October 2002). Regarding claim 1, Christians et al teach a process for the reverse transcription and/or amplification of a product of a reverse transcription of a pool of nucleic acids of a type (A) from a biological sample or an enzymatic reaction, said process comprising selectively suppressing the reverse transcription of at least one unwanted nucleic acid of type (A) and/or selectively suppressing the amplification of a product of a reverse transcription of at least one unwanted nucleic acid of type (A) (see abstract, Figure 1 and paragraphs 0002,0031, and pages 4-6).

Regarding claim 2, Christians et al teach the process according to claim 1, wherein the nucleic acid of type (A) is mRNA (0029).

Regarding claim 3, Christians et al teach the process according to claim 1, wherein the unwanted nucleic acid of type (A) is an mRNA which has a proportion of 20% or more of the total mRNA (0029 and 0045).

Regarding claim 4, Christians et al teach the process according to claim 1, further comprising the following steps a) carrying out a reverse transcription reaction of an RNA from a biological sample or a enzymatic reaction in the presence of at least one oligo-dT primer, b) optionally after step a) carrying out a cDNA second strand synthesis, c) optionally after step b) purifying the ds-cDNA while simultaneously depleting all the single-stranded nucleic acids from the reaction product of step b), d) optionally after step a) and/or b) and/or c) carrying out amplification of the cDNA (0067-0075 and page 11-12).

Regarding claim 5, Christians et al teach the process according to claim 4, wherein steps a) and/or d) are carried out in the presence of at least one molecular species for selectively suppressing the reverse transcription of at least one unwanted mRNA, while the molecular species prevents the reverse transcription of the unwanted mRNA, and/or for selectively suppressing the amplification of a product of the reverse transcription of at least one unwanted mRNA, the molecular species preventing the amplification of the single-stranded or double-stranded cDNA prepared from the unwanted mRNA (Figure 1 and 0065).

Regarding claim 6, Christians et al teach the process according to claim 1, wherein in the reverse transcription reaction a reverse transcriptase with an intrinsic RNase H activity is used (0007 and 0045)

Regarding claim 7, Christians et al teach the process according to claim 1, wherein the biological sample is whole blood, or it is a sample contaminated with whole blood (0068)

Regarding claim 8, Christians et al teach the process according to claim 7, wherein the biological sample is whole blood, and that the whole blood is taken up and/or stored in a stabilizing reagent (0039)

Regarding claim 9, Christians et al teach the process according to claim 8, wherein the stabilizing reagent is contained in a blood sample vial and the blood is transferred into the stabilizing reagent immediately after being taken (0039-0040).

Regarding claim 10, Christians et al teach the process according to claim 8, wherein the stabilizing reagent contains a tetra-alkyl-ammonium salt in the presence of an organic acid (0040)

Regarding claim 11, Christians et al teach the process according to claim 8, wherein the stabilizing reagent contains at least one guanidine compound, a buffer substance, a reducing agent and a detergent (0040).

Regarding claim 12, Christians et al teach the process according to claim 1, wherein the biological sample is whole blood, and that the unwanted nucleic acid of type (A) is globin-mRNA (Figure 1 and 0003 and 0048 and 0067).

Regarding claims 17 and 19, Christians et al teach the process according to claim 5, wherein the molecular species is a DNA oligonucleotide and/or RNA oligonucleotide complementary to the mRNA (0050 and 0065).

Regarding claim 18, Christians et al teach the process according to claim 17, wherein the molecular species has a length of 10 to 60 nucleotides, preferably 12 to 30 nucleotides (0090, SEQ ID NO: 1-3). .

Regarding claim 24, Christians et al teach the process according to claim 17, wherein the molecular species binds in the 3' region of the mRNA or one of the cDNA strands (0090).

Regarding claim 25, Christians et al teach the process according to claim 5, wherein a number of molecular species are used which are complementary to different regions of one or more specific mRNA(s) or at least one strand of one or more specific cDNA(s) (0090).

Regarding claim 26, Christians et al teach the process according to claim 5, wherein at least one molecular species is used which is complementary to a homologous region of different mRNAs or cDNAs (0090, see sequences for Alpha 1 and alpha 2)..

Regarding claim 27, Christians et al teach the process according to claim 5, wherein the molecular species has at its 3' end a modification which prevents elongation from being initialized at the 3' end of the molecular species (0070).

Regarding claim 39, Christians et al teach the process according to claim 1, wherein the amplification comprises (0059).

Regarding claim 40, Christians et al teach the process according claim 39, wherein the in vitro transcription is followed by a DNase digestion as well as purification of the cRNA (0052, 0059, 0093-0094). Therefore, Christians et al meet the limitations of the claims recited above.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 13-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Christians et al as previously applied above in view of Bair, JR et al (20040019196,

04/2003) and Hillbrand et al (WO 9534569). Regarding claims 14-16, Christians et al teach a method of suppressing reverse transcription to remove unwanted nucleic acid from a population of molecules as previously described above. Christians et al also teach wherein the target nucleic acid molecules are isolated and purified from a blood sample using chaotropic agents and solid support (0061, 0072, 0074, 0086, 0090).

Christians et al do not expressly teach wherein the purification of the nucleic acid comprises using silica particles. Christians et al also does not teach the concentration of the buffer solution comprising the guanidine compound. However, these claims merely recite a plethora of conventional nucleic acid manipulation reagents and methodologies, as well as well as routine optimization or reaction components, concentrations, and parameters. Clearly such conventional and trivial modification and optimizations do not contribute towards patentability as these conditions are commonly applied and well known in the prior art. For example, Bair JR et al cites examples of using a combination of chaotropic substances such as guanidine isothicyanate, guanidine, guanidine hydrochloride, and urea mixtures at ionic strengths greater than 4M in conjunction with silica based carriers as a means of purifying nucleic acids (0010). Bair et al cites Hillebrand et al as an express teaching of this combination. Thus, one of ordinary skill in the art would have been motivated to modify the primary references in the manner of the claims to achieve the expected benefits, optimizations an/or expanded applications. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to carry out the claimed methods.

11. Claims 21-23 and 28-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Oemar et al as previously applied above in view of Christian et al as previously applied above. The claims 21-23 and 28-32 recite a plethora of conventional nucleic acid manipulation reagents and methodologies, as well as well as routine optimization or reaction components, concentrations, and parameters. Clearly such conventional and trivial modification and optimizations do not contribute towards patentability as these reagents are well known in the art as blockers or cleavage agents which inhibit or suppress amplification reactions or cleave unwanted nucleic acid sequences. See e.g., the teaching of Christians et al and Oemar et al which provides examples of oligonucleotides which block or suppress amplification and notes the use of enzymatic cleavage agents for removing unwanted nucleic acids. Thus, one of ordinary skill in the art would have been motivated to modify the primary references in the manner of the claims to achieve the expected benefits, optimizations an/or expanded applications, using different reagents with similar properties. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to carry out the claimed methods in the absence of secondary consideration.

12. Claim 33 is rejected under 35 U.S.C. 103(a) as being unpatentable over Christian et al as previous applied above in view of Kmiec et al (US 2003/0051270, effective filling date March 2000) and further in view of Buck et al (Biotechniques, vol. 27, pages 528-536, September 1999). Regarding claim 33, Christians et al teach a process for the reverse transcription and/or amplification of a product of a reverse transcription of a pool of nucleic acids of a type (A) from a biological sample or an enzymatic reaction,

said process comprising selectively suppressing the reverse transcription of at least one unwanted nucleic acid of type (A) and/or selectively suppressing the amplification of a product of a reverse transcription of at least one unwanted nucleic acid of type (A) (see abstract, Figure 1 and paragraphs 0002, 0031, and pages 4-6). Christian et al further teaches wherein the molecular species is a DNA oligonucleotide and the globin mRNA embodies an alpha 1 globin and/or alpha-mRNA, the DNA oligonucleotide comprising a sequence selected from SEQ ID NO: 1 and 2. Christian does not expressly teach wherein the sequence comprises the sequence of SEQ ID NO: 2 or 3 as claimed in the instant invention.

Kmeic et al teaches a sequence comprising the sequences of SEQ ID NOS: 2 and 3 that is substantially identical, wherein these sequences are a hemoglobin variant sequence (see page 122, sequence lines 1 and 2 of SEQ ID NO: 2953).

In the court decision *In Re Deuel* 34 USPQ 2d 1210 (Fed. Cir. 1995), the Court of Appeals for the Federal Circuit determined that the existence of a general method of identifying a specific DNA does not make the specific DNA obvious. Regarding structural or functional homologs, however, the Court stated,

"Normally, a *prima facie* case of obviousness is based upon structural similarity, i.e., an established structural relationship between a prior art compound and the claimed compound. Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologs because homologs often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties (see page 9, paragraph 4 of attached ref)."

Since the claimed primers and probes simply represent structural homologs, which are derived from sequences of globin genes suggested by the prior art as useful

as oligonucleotides and concerning which a biochemist of ordinary skill would attempt to obtain alternate compounds with improved properties, the claimed primers and probes are *prima facie* obvious over the cited references in the absence of secondary considerations.

Conclusion

13. No claims are allowed. Any inquiry concerning this communication or earlier communications from the examiner should be directed to CYNTHIA B. WILDER whose telephone number is (571)272-0791. The examiner can normally be reached on a flexible schedule.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/CYNTHIA WILDER/
Patent Examiner, Art Unit 1637